REMARKS

Claims 1 – 9, 11, 12, 16 – 38, and 51 – 71 have been cancelled. Claims 10, 43, 72 and 73 are amended, and new claims 74 – 76 are added.

Claims 10, 13 – 15, 39 – 50, and 72 – 76 are now pending.

In the Office Action, claims 10, 13 – 15, 39 – 42 and 73 were rejected under §112, first paragraph, for allegedly failing to comply with the written description requirement. To the extent this rejection may apply to the present claims, it is respectfully traversed.

It is asserted in the rejection that SEQ ID NO:3 is a coding sequence. However, SEQ ID NO:3 also includes eleven nucleotides 5' to the ATG initiating methionine encoding codon which marks the beginning of the AAH coding sequence. As is well known in the art, 5' regulatory nucleic acid sequences of a cDNA (SEQ ID NO:3) are untranslated nucleotides such as promoter elements.

Claim 10 has now been amended to recite a 10 nucleotide sequence that is complementary to is a portion of the 5'untranslated or regulatory sequence of SEQ ID NO:3 (i.e, the eleven nucleotides 5' to the underlined initiating codon in SEQ ID NO:3). Other claims require (e.g., 43, and 72-75) require that the length of the antisense sequence consist of between 10-20 or 10-50 nucleotides. Written description for these finite sequences is provided in Table 2 (HAAH cDNA; SEQ ID NO:3) of the specification. In view of the amendment, this rejection should be reconsidered and withdrawn.

The only other issue remaining in this application is the rejection of all of the previously pending claims under §112, first paragraph, for nonenablement. To the extent this rejection may be applicable to any of the presently pending claims, it is respectfully traversed.

First, the publications cited are of a review nature on the status of gene therapy as of 1995, 1996 and 1997. The present application was filed in 1999. Second, the publications are either entirely or substantially concerned with gene therapy involving expression of protein from a transferred gene, a result requiring stable integration an entire gene and sustained expression of protein. Thus, the problems addressed in the references concern targeted *in vivo* delivery of genes and expression of proteins. All of the examiner's comments appearing from page 3, second paragraph to page 4, end of second paragraph, only raise issues in the references having to do with integration of a whole gene and its adequate expression of *protein*. Applicants emphasize that the antisense nature of the presently claimed methods does not involve protein expression at all. Rather, the claimed antisense methods reduce the aberrant overexpression of AAH in malignant neoplasms. This aspect of the present invention is not addressed at all in the cited references. This is because the present invention, for the first time ever, encompasses the discovery of a protein vastly overexpressed in malignant cells and for which if reduced or interfered with (for example, by antibodies or antisense) decreases motility and invasiveness of the cells and change the morphology to that more characteristic of normal cells (see, for instance, Example 5 of the Specification).

In fact, the only mention of antisense Applicants could find in the papers cited is in Orkin et al., and only with respect to HIV (7^{th} page), where it states that a handful of

vaccination trials were ongoing (as of 1995), some of which involved *ex vivo* treatment of CD4 cells with antisense RNA that blocks translation of HIV gene products.

The examiner asserts that Orkin teaches that it is necessary to target expression of transferred genes by means of regulatory sequences in transfer vectors, and that Applicants have not taught such vectors. However, again, the present invention is not concerned with expression of *proteins* in targeted cells, and thus such regulatory sequences are not required. In fact, all that the claims require is delivery of antisense to mammalian tumor cells, which can be done in its most basic respect with essentially naked nucleic acid (see page 18, line 33, of the specification), or transcribed from a vector containing the appropriate nucleic acid. For example, as stated in the Specification, DNA containing a (tissue-specific or tumor-specific) promoter operably linked to a DNA (antisense) template is used to transcribe the antisense RNA in the cells, and numerous standard delivery systems, e.g., well-known viral vectors such as adeno- and adeno-associated viruses, are described in the Specification (page 18, line 29, to page 19, line 14).

It is respectfully submitted that antisense therapy, as opposed to gene therapy, was much further developed at the time of the present invention. In fact, as Applicants have mentioned in a previous response, the FDA approved its first antisense "drug" in 1998 (Isis Pharmaceuticals). See further, the remarks in Applicants' response of July 19, 2001, Declaration of Dr. Wands and accompanying Attachments. The extensive guidance in the Specification, the further evidence provided by the Declarations of Dr. Wands, and the state of the art the art at the time of the present invention all support the enablement of the claims.

The rejection fails to establish that the claimed invention is not enabled.

Accordingly, the rejection should be withdrawn.

CONCLUSION

Applicants respectfully submit that claims 10, 13 – 15, 39 – 50, and 72 – 79 are in condition for allowance. Prompt issuance of a Notice of Allowance is earnestly solicited. The Examiner is invited to contact the undersigned at the number or email listed below should she believe there are any remaining issues that could be more easily resolved by personal or telephonic interview.

A petition for extension of time and a check in the amount of $ 60.00 is enclosed to cover the petition fee for a one-month extension of time pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21486-032.

Respectfully submitted,

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